Supplements for Research on Image-Guided Interventions in SPOREs and Cancer Centers
(IGI Supplemental Awards)
Guidelines for Application, Review, and Award
(12/2004)

Purpose

These guidelines describe the application for, and review of, administrative supplements to NCI SPORE programs and NCI-designated Cancer Centers (*IGI Supplemental Awards*) for pre-clinical and early translational studies of oncologic image-guided interventions (IGIs).

Oncologic IGIs include regional and local therapies, guided by real-time imaging, with the common aim of tumor destruction. End effectors of therapeutic IGIs include a variety of techniques such as radiofrequency (RF) energy, laser light, high-intensity focused ultrasound (HIFU), cryoablation, direct injection, transarterial chemoembolization (TACE), and other local and regional methods. All involve visual and other forms of feedback, iterative modulation of treatment, and ultimately determination of procedure endpoints.

IGI Supplemental Awards are intended to facilitate the development, validation, and optimization of oncologic IGI methods, as well as the identification of promising, clinically safe and feasible new oncologic IGIs that warrant subsequent multi-center clinical investigations. The ultimate clinical aims of oncologic IGIs range from cure of early stage disease and pre-cancer to palliation of advanced disease. Projects considered to be responsive include, but are not limited to the following:

1) Pre-clinical or early clinical translational studies that exploit tumor characteristics (molecular, cellular, pathophysiologic, physical, anatomic) in the design, development, and testing of one or more of the following components of an IGI: real-time imaging/sensing; image-processing; navigation; treatment/ablation; feedback/modulation/control (operator, semi-automated, or automated; unassisted or robotic);

2) Studies employing novel real-time fusion methods of imaging/sensing in IGI. Examples include integration of traditional anatomic imaging modalities such as CT, ultrasound, MRI, and fluoroscopy with others, such as molecular imaging, pathophysiologic imaging (e.g., hypoxia), spectroscopy (MR or optical) or elastography (MR or ultrasound).

3) Validation studies aimed at establishing imaging equivalents of the surgically proven "tumor-free margin." Today oncologic IGI encompasses surgical, endoscopic, percutaneous, and completely noninvasive approaches. But studies seeking imaging equivalents of the "tumor-free margin" are considered potentially fundamental enablers of entirely non-surgical image-guided tumor destruction. Such studies represent a particularly high priority, as the nation is anticipating a great increase in the number of screen-detected early-stage cancers.

4) Studies exploiting a combination of technologies to effect a therapeutic intervention. Examples include therapeutic nanocarriers that are activated at the tumor site by local application of RF, HIFU, or other forms of energy; liposomal, encapsulated, or otherwise-modified

chemotherapeutic drugs that are activated or potentiated at the tumor site by RF, HIFU or other energy application; combinations of local or regional tumor ablation and radiotherapy; etc.

Collaboration between investigators of the SPORE or Cancer Center and their basic science and engineering colleagues, both within and outside of the institution, and industry when appropriate is encouraged.

The inclusion of minorities or individuals from underserved populations as participants in the study and the involvement of a junior clinical investigator (Instructor, Assistant Professor, and Research Assistant Professor) in its design and execution are encouraged. Junior investigators with appropriate qualifications are eligible to serve as Principal Investigators.

Projects *not* considered to be responsive include the following:

1) Studies at an advanced stage of clinical investigation, including most multi-center trials;

2) Studies of oncologic imaging alone, without a clear link to IGI;

3) Studies involving pre-intervention imaging for treatment planning, but no real-time or iterative therapeutic component;

4) Projects involving requests for grant support of capital equipment procurement in excess of $15,000 for one-year awards or $25,000 for two-year awards.

Questions regarding responsiveness of proposed projects to this initiative should be directed to the Program personnel listed below.

Eligibility

Eligible applicants include all SPORE investigators and Cancer Center investigators, their co-investigators, and clinical and basic scientists in other departments of the institution. Each application must meet the above criteria for project responsiveness and be approved for submission by the SPORE or Cancer Center Director.

Type and Number of Applications That May Be Submitted

A SPORE or Cancer Center may submit:

1) One application involving a study that is exclusive to its own SPORE or Cancer Center, or

2) One application involving a collaborative study with another SPORE or Cancer Center, or

3) Two applications, one of which involves a study exclusive to its own SPORE or Cancer Center and one of which is collaborative with another SPORE or Cancer Center, or

4) Two applications, both involving collaborative studies with other SPOREs or Cancer Centers.

If a collaborative study between two SPOREs or Cancer Centers is being proposed, each SPORE or Cancer Center must submit an independent application and budget request. If justified, collaborations with other institutions (and co-investigators) that do not have a SPORE or Cancer Center award may be proposed. In this case, the activities performed by an outside co-investigator(s) requiring financial support should be incorporated as a subcontract into the application submitted by the SPORE or Cancer Center. See sections on Allowable Costs and Application Procedures below.

Receipt Date

The receipt date for applications is **June 1, 2005**.

Allowable Costs

If one application is submitted, the request cannot exceed a maximum of $250,000 in total costs (direct plus indirect) per participating SPORE or Cancer Center per year for a period of up to two years. The total cost for 2 years may not exceed $500,000. If two applications (one institutional and one collaborative, or two collaborative) are submitted, then the combined total cost for *both* applications cannot exceed $350,000 per year. The combined total cost for both proposals over two years may not exceed $700,000. The following table is provided to clarify the allowable costs for institutions submitting more than one application. The one-year budget examples provided below are not all inclusive; additional budget scenarios are acceptable as long as they do not exceed the caps.

Collaborations	Project #1	Project #2	Project #3	*Institution Total*
Institution A	$250,000	$100,000		$350,000
Institution B	$100,000		$150,000	$250,000
Institution C		$250,000	$75,000	$325,000
Institution D			$100,000	$100,000
Project Total	$350,000	$350,000	$325,000	

In the above tabular illustration, Institution A is at the budgetary cap.

Collaborative projects involving more than two SPOREs, two Cancer Centers, or one SPORE and one Cancer Center should be discussed in advance with the NCI *IGI Supplemental Awards* Program Director listed below.

Central coordination of submissions by the SPORE Director, his/her designee, Cancer Center Director, or his/her designee is essential, especially if the SPORE or Cancer Center is submitting two applications. Budgets for each must be negotiated to ensure that total costs for both applications do not exceed $350,000 per year and that funds are fairly appropriated to each proposed project.

Research or clinical activities performed outside of a SPORE or Cancer Center can be included as subcontracts on a project, but count towards the total cost cap for the parent institution. Funds may be used for any clinical or laboratory activity pertinent to the intervention. It is not the intent of these awards to fund large capital equipment (in excess of limits cited above) or duplicate resources already

available within a SPORE or Cancer Center. Investigators should make maximum use of resources already available within their institution. All applicable NIH policies must be followed.

Please note that costs to include the participation of underserved populations or minorities in the study (e.g., travel expenses, patient navigators, case managers, or translators), if possible, are allowable and encouraged. Requests to support the partial salary and/or research activities of a junior clinical investigator are also encouraged. Special populations include government-designated ethnic and racial groups, including American Indian or Alaska Native; Asian; African American; Hispanic or Latino; and Native Hawaiian or other Pacific Islander. The NCI's working definition of "special populations" also includes medically underserved populations, such as rural, low-income, and low-literate individuals. These groups are generally characterized as experiencing higher cancer incidence and/or mortality rates or have inadequate access to, or reduced utilization of, high-quality cancer prevention, screening, and early detection, treatment, and/or rehabilitation services.

Letter of Intent to Submit an Application

To expedite the review process, you are requested to notify the Image-Guided Intervention Branch of the Cancer Imaging Program, Division of Cancer Treatment and Diagnosis, NCI of your intent to submit an application(s) for this administrative supplement. **This notification should be provided either by e-mail or letter by no later than May 1, 2005 to:**

Keyvan Farahani, Ph.D., Program Director
NCI/DCTD/CIP/IGI Branch
6130 Executive Blvd.
Room 3006
Rockville, MD 20852 (courier)
Bethesda, MD 20892 (if US Postal Service)
farahani@nih.gov

The letter of intent to submit an application MUST: 1) be copied to the NCI Program Director responsible for the applicant's SPORE or Cancer Center, 2) include the SPORE or Cancer Center grant number, 3) include the full name, address, phone and e-mail contact information for the responsible NCI Program Director, and 4) briefly describe (one paragraph) the proposed research and the responsiveness of the research to the *IGI Supplemental Award* initiative.

Application Procedures

1) Cover Letter:

A **cover letter** should accompany each application and be addressed to Dr. Farahani. The cover letter must: 1) request an *IGI Supplemental Award*, 2) provide the SPORE or Cancer Center grant number, 3) provide the full name and contact information for the NCI Program Director responsible for the SPORE or Cancer Center, and 4) be signed by the applicant's SPORE or Cancer Center Director, the leader of the project, and the appropriate business official of the institution.

2) Where to Send the Cover Letter and Application:

The cover letter and six copies of each application should be sent to:

Keyvan Farahani, Ph.D., Program Director
NCI/DCTD/CIP/IGI Branch
6130 Executive Blvd.
Room 3006
Rockville, MD 20852 (courier)
Bethesda, MD 20892 (if US Postal Service)
farahani@nih.gov

Note: No signatures are required on electronic files. The documents must be in MS Word format and PC compatible. A contact phone number and e-mail address for the project leader must also be provided.

3) Format for the Application:

- Use the standard **face page** of the PHS 398 (09/2004) form and follow instruction accordingly. For Item 2, check "yes" and provide the title "*IGI Supplemental Awards."* In Items 7A through 8b, denote the direct and total costs for the first year, as well as for the entire period of support. Total costs should not exceed those stated under Allowable Costs above. The SPORE Director or Cancer Center Director and Business Official of the institution must sign the face page.

- Use the standard **budget pages** of the PHS 398 (09/2004) application (form pages 4-6). Provide a budget justification for personnel, supplies, patient-associated costs, and other expenses. List any additional sources of support for the trial provided by the SPORE grant, the Cancer Center grant, research grants, or other outside entities such as pharmaceutical or device manufacturers.

- Provide **biographical sketches** of key personnel, using the standard PHS 398 (09/2004) format.

- Continuing with the PHS 398 (09/2004), **in 10 pages or less,** provide a **summary** that includes the following:

    - Hypothesis to be tested
    - Significance and innovativeness of the work
    - Brief statement describing how the proposed research is responsive to the *IGI Supplemental Award* initiative
    - Brief description of research that led to the proposed work
    - A detailed description of the Research Plan
    - Documentation of available resources, facilities, laboratories, etc.

- For clinical studies, documentation of available patient population
- For clinical studies, a plan for gender and minority inclusion and accrual, in accordance with NIH policy
- A description and justification for the statistical design, as appropriate
- If applicable, a plan for the support and mentorship of a junior clinical investigator

4) Additional Required Documentation. *Since it is the intent of this program to award funds for immediate use, applications will not be reviewed until all required materials have been received.*

For clinical studies:

- Complete clinical protocol and copies of informed consents

- Approval by the SPORE or Cancer Center's Protocol Review and Monitoring System (PRMS) or equivalent monitoring body

- A Data and Safety Monitoring Plan (DSMP). This may the institutional DSMP approved by the NCI, with modifications appropriate to the study proposed. Applicants are encouraged to refer to and follow the "Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials", which may be found at http://deainfo.nci.nih.gov/grantspolicies/datasafety.htm.

- Additional guidance is available at http://www.cancer.gov/clinicaltrials/conducting/dsm-guidelines.

- Availability of device(s) being tested and verification of an existing IDE (or, in the case of drugs or biologicals, an existing IND) held by the institution or commercial source. NCI expects that the participating institutions or companies will assume the regulatory responsibility for any investigational drugs, biologicals, or devices that will be tested in a clinical setting. If using NCI sponsored agents, documentation of approval by the NCI Protocol Review Committee should be provided.

- Certification that all individuals involved in the design and conduct of the trial have completed education in the protection of human subjects in accordance with the NIH policy, "Required Education in the Protection of Human Research Participants", as announced in the June 5, 2000 NIH Guide (revised August 25, 2000) (http://grants.nih.gov/grant/guide/notice-files/NOT-OD-00-039.html). It is not necessary to submit certification for any individual for whom certification has already been provided on the parent grant.

5) Inter-SPORE and SPORE-Cancer Center Collaborations:

For Inter-SPORE and SPORE-Cancer Center Collaborations, only the lead institution is required to submit a full application that details the overall goal of the study and project activities performed at its site. Participating institutions should submit a shorter application limited to a description of activities at their own specific sites. For clinical studies, a protocol should be submitted from the participating institution only if it differs from that submitted for the lead institution. All other materials that differ

between the lead and participating institution(s) (e.g., budgets, IRB approvals, etc.) should also be submitted by the participating institution(s).

Review of the Application

A committee of NCI program staff will evaluate the merits of applications using external basic or clinical/translational experts, when additional expertise is needed, based upon the following review criteria:

- Scientific merit
- Innovation
- Significance
- Feasibility for completion in two years or less
- For animal studies, adequacy of the plan for protection of animal subjects
- For clinical studies, adequacy of the plan for protection of human subjects
- For clinical studies, adequacy of the plan to include minorities and underserved populations, to the extent possible within the applicable eligibility criteria
- Inclusion of a plan to involve a junior investigator(s)

Awards

It is the intent to select meritorious applications for funding within 90 days of the application receipt date based on recommendations by the NCI.

Date

Name of Cancer Center Director
Institution
Address
City, State, Zip

Cancer Center Grant #

Dear Dr._____:

Enclosed please find the announcement of a special one-time award opportunity entitled, "Supplements for Research on Image-Guided Interventions in SPOREs and Cancer Centers" *(IGI Supplemental Awards)*. The main purpose of these awards is to facilitate the development and early translation to humans of research on image-guided interventions in oncology.

The announcement details eligibility criteria and criteria for responsiveness of proposals. All SPORE investigators and Cancer Center investigators, their co-investigators, and clinical and basic scientists in other departments of the institution are eligible. Each application must meet the specific responsiveness criteria and be approved for submission by the SPORE or Cancer Center Director.

Please note that the one-time receipt date is June 1, 2005, and that a letter-of-intent to submit a proposal is due by May 1, 2005.

The NCI encourages you to share this opportunity with your co-investigators and collaborators, as well as with qualified potential investigators and collaborators in other departments. It is appropriate to share it with all individuals in your institution who are engaged in research that meets the responsiveness criteria on the first page of the announcement.

Please contact Dr. Becker at the email address or phone number below if you have questions regarding this initiative.

Sincerely,

Linda Weiss, Ph.D., Chief
Cancer Centers Program
301-496-8531
WeissL@mail.nih.gov

Gary J. Becker, M.D., Branch Chief
Image-Guided Intervention/CIP/DCTD
301-451-2669
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